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EXAMINER

BORIN, MICHAEL L

ART UNIT PAPER NUMBER

1631

DATE MAILED: 01/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/747,174

Applicant(s)

SEM ET AL.

Examiner

Michael Borin

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 18 October 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19 and 21-23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19 and 21-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- ☐ Interview Summary (PTO-413) Paper No(s). _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

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DETAILED ACTION

1. Response to notice of non-responsive communication filed 10/18/2003 is acknowledged.

Status of Claims

2. Claims 1-18,20,24-44 are canceled. Claims 19,21-23 are pending.

The claims are addressed to the extent they read on the elected species, NAD-related molecules.

Claim Rejections - 35 USC § 112, second paragraph

3. Claims 19, 21-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is made for the following reason:

A. Claim 19: parts c) and (d) of the claim address first and second bound conformations of the ligand. However, the preceding part (a) of the claim addressed "at least" first and second bound conformations, meaning that there may be more than two bound conformations; steps c) and (d) do not address these other conformations.

B. Part (d) of claim 19 lacks internal antecedent basis because the middle of the step addresses "conserved atoms" while beginning of the step uses the term "conserved" in regard to locations, rather than particular atoms.

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Claim Rejections - 35 USC § 103.

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 19-23 are rejected under 35 U.S.C. 102(b) as obvious over Carugo et al. (Proteins:Structure, Function and Genetics 28: 10-28, 1997).

The instant claims are drawn to method of identifying polypeptide pharmacofamilies¹ exhibiting binding specificity to different conformations of a ligand. Pursuant to the election of species, the ligand species under consideration are nicotine amide-related molecules. The method includes the steps of identifying various conformations of the ligand in its complexes with different polypeptides of a polypeptide family², and identifying more than one of said various conformations of the ligand in its complexes with different polypeptides by the conserved location of ligand's atoms in three-dimensional space, and thereby identifying polypeptide

¹A peptide pharmacofamily is defined as a population of polypeptides that bind to the ligand (nicotine amide-related molecule) such that the latter is substantially the same conformation in complexes with all peptide members of pharmacofamily.

²A polypeptide family encompasses any peptides capable of binding to the given ligand (see p. 15).

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pharmacofamilies as groups of polypeptides as having binding specificity to a particular conformation of the ligand.

Carugo et al. examines complexes of NAD and NADP with various polypeptides.

The study examines conserved interactions of ligands and peptides by systematic analysis of crystal tertiary structures of ligands, i.e., conserved locations of ligand's atoms in three-dimensional space. In particular, the study describes 13 different NADP conformations (Fig. 3), and identifies groups of polypeptides having binding specificity to a particular conformation of NADP (Fig. 2). For example, cluster 1 (which reads, using the language of instant claims on pharmacofamily 1) includes malate-, lactate-, alcohol-, formate-dehydrogenases, etc (see Fig. 2 and p. 12). The referenced method reads on the claimed method of identifying polypeptide pharmacofamilies.

As Carugo et al reference demonstrates specific NADP conformations with conserved tertiary structures, and identifies groups of polypeptides having binding specificity to a particular conformations of NADP, it would be *prima facie* obvious to one skilled in the art at the time the invention was made to be motivated to determine conserved coordinates for polypeptides interacting with a given bound conformation of the ligand, because determination of such coordinates specific for particular group ("pharmacofamily") of polypeptides is essential for understanding mechanisms of

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protein/ligand interaction and desirable for design of potential pharmacophores. Further, as proteins normally interact with ligands via hydrogen bonds, it would be obviously to classify interacting atoms as hydrogen bond donors or acceptors.

Claim Rejections - 35 USC § 112, first paragraph.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 19, 21-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Claim 19 introduces new matter is claims the step of determining particular "conserved atoms" that are conserved between polypeptides of given pharmacofamily and are specific to the specific bound conformation of the ligand. Specification does teach determining peptide residues located around given bound conformation of the ligand (e.g., Fig. 3, Tab. 3D), but do not teach that the peptide atoms are specific for one conformation vs. another, or determining such specificity of peptide's atoms.

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6. Claims 19,21-23 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method as claimed using NADP, does not reasonably provide enablement for utilizing other nicotine amide-related molecules as ligands. The rejection is maintained for the reasons of record and further in view of the following.

Examiner agrees with applicant's analysis of Bellamacina reference. The reference does not clearly show difference between different NAD containing molecules, much the same as the specification which, in Example 1, addresses all molecules together. However, the Carugo reference is much more specific in demonstrating clear distinction between variability of protein-cofactor interactions for NADP complexes, and lack thereof for NAD complexes which are the same for all complexes. The reference teaches that despite their great structure similarity with NADP differing from NAD only by presence of an additional phosphate group, NAD and NADP differ substantially in their biochemistry, and their small difference provides one of the most striking examples of the power of molecular recognition in biological chemistry (see Introduction section). The reference then demonstrates 13 different bound conformations for NADP, discusses that NADP shows a bigger conformational freedom than NAD, and teaches that NAD and NADP never cluster together (p. 12).

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Examiner considers Carugo reference as clearly teaching that while NADP can accept a variety of conformations when bound to different polypeptides, conformation of NAD is well conserved and does not change significantly upon binding to various polypeptides. It is noteworthy that applicant did not provide any comments about the reference other than restating the position of the Examiner.

Turning to specification, is not quite clear what ligand is addressed in either Figures or Examples. It seems, however, that although different NAD-related molecules were used in database search (p. 71, lines 10-14), the analysis of results was focused on complexes of NADP - see p. 72, line 10 +, or Table 11, addressing NADP complexes.

Therefore, Examiner maintains that as there are no working examples or guidance on how to practice the invention with nicotine amide-related molecules other than NADPH, and with the insufficient guidance regarding identification pharmacofamilies for nicotine amide-related molecules other than NADPH and in view of unpredictability and the state of art one skilled in the art could not make and/or use the invention with the claimed breadth without an undue amount of experimentation.

Conclusion.

7. No claims are allowed.

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8. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (703) 305-4506. Dr. Borin can normally be reached between the hours of 8:30 A.M. to 5:00 P.M. EST Monday to Friday. If attempts to reach the examiner by telephone are

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unsuccessful, the examiner's supervisor, Mr. Michael Woodward, can be reached on (703) 308-4028. The fax telephone number for this group is (703) 305-3014.

Any inquiry of a general nature or relating the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

January 20, 2004

mlb

A handwritten signature in black ink, appearing to read 'Michael Borin', with a long, sweeping horizontal stroke extending to the right.

MICHAEL BORIN, PH.D
PRIMARY EXAMINER